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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/695,423	10/25/2000	Masaru Kato	049441/0124	2544

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EXAMINER
RAO, MANJUNATH N

ART UNIT	PAPER NUMBER
1652	14

DATE MAILED: 04/18/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/695,423	KATO ET AL.	
	Examiner	Art Unit	
	Manjunath N. Rao, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 January 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-43,123-128,147 and 150-153* is/are pending in the application.

4a) Of the above claim(s) *38-43 and 147* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-37,123-128 and 150-153* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 25-43, 123-128, 147, 150-153 are still at issue and are present for examination. Claims 25-37, 123-128, 150-153 are now under consideration. Claims 38-43, 147 remain withdrawn from consideration as being drawn to non-elected invention.

Election/Restrictions

Applicants continue to traverse the restriction and request the Examiner to rejoin claims 38-43 and 147 drawn to the method of making the enzyme claimed. Such rejoinder will be considered by the Examiner when claims now under consideration are in condition for allowance. Until such time claims 38-43 and 147 will remain withdrawn from consideration.

Applicants' amendments and arguments filed on 1-24-03, paper No.11, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Specification

The amendment filed on 1-24 -03 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: Applicants amend claim 30, part 3, broadening the pH stability within the range from 3.0 to 13.0. Examiner views this broadening of the pH range as new matter. A perusal of the specification at page 107, and figure 13, which describes

the pH stability characteristic of the claimed amylase indicates that the enzyme is active in the pH range of 3.0 to 11. The enzyme appears to be totally inactive at pH 12.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Objections

Claim 30 is objected to because of the following informalities: Claim 30, part 3, claims that the enzyme is stable within the range from pH 3.0 to pH 13.0. However a perusal of the specification at figure 13 indicates that the enzyme becomes totally inactive at pH 12.0. Therefore, there exists an inconsistency between what is described in the specification and what is claimed. Appropriate correction is required.

Claim 37 is objected to as being dependent on a rejected claim. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 30 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicants amend claim 30, part 3, broadening the pH stability within the range from 3.0 to 13.0. Examiner views this broadening of the pH range as new matter. A

perusal of the specification at page 107, and figure 13, which describes the pH stability characteristic of the claimed amylase indicates that the enzyme is active in the pH range of 3.0 to 11. The enzyme appears to be totally inactive at pH 12. Applicant is required to cancel the new matter in the reply to this Office Action.

Claims 25-36, 126-128, 150-153 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an enzyme with SEQ ID NO:6 or 8, encoded by a polynucleotide with SEQ ID NO:5 or 7 respectively, which is isolated from an archaebacterium belonging to genus *Sulfolobus solfataricus* and which acts on a substrate saccharide composed of at least three sugar units wherein at least three sugar units from the reducing end are glucose residues so as to liberate principally monosaccharides and/or disaccharides by hydrolyzing the substrate saccharide from the reducing end side, does not reasonably provide enablement for all such polypeptides isolated from all other sources including variants, mutants and recombinants or such polypeptides encoded by polynucleotides which hybridize with SEQ ID NO:5 or 7 at 65° C in 6XSSPE and 0.5% SDS followed by washing with a solution comprising 2X SSPE and 0.1% SDS for 10 min, twice. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the

prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 25-36, 126-128, 150-153 are so broad as to encompass any amylase which acts on a substrate saccharide composed of at least three glucose sugar units from the reducing end and liberates monosaccharides and /or disaccharides and shows a trehaloseoligosaccahride-hydrolyzing activity with some characteristics as described in above claims including variants , mutants and recombinants. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the amino acid sequence of only two such polypeptides isolated from archaebacterium *Sulfolobus* sp.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art

would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompasses all polypeptides with above activity including mutants, variants and recombinants because the specification does not establish: (A) a rational and predictable scheme for isolation and characterization of the above enzyme from any or all sources including any microbe, plant or animal; (B) regions of the protein structure which may be modified without effecting its activity; (C) the general tolerance of such polypeptides to modification and extent of such tolerance; (D) a rational and predictable scheme for modifying any residue in those polypeptides with an expectation of obtaining the desired biological function; and (E) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including polypeptides from all or any source including variants, mutants and recombinants. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of the intended polypeptides having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

In response to the previous Office action, applicants traverse the above rejection and argue that the specification describes in Examples II-2 and II-4 the isolation of the amylase from three sources belonging to the genus *Sulfolobus* including purification and activity measurements. Applicants also argue that Table 12-14 shows the trehaloseoligosaccahride-hydrolyzing activity of the enzyme activity and the specific activity of the DEAE ion-exchange chromatography purified enzyme to be 10.6 units/mg. Applicants also argue that contrary to Examiner's allegation they have disclosed only two species of the polypeptides and they have disclosed modified polypeptides and refer to pages 56-57. Examiner respectfully disagrees with such arguments and asserts that such arguments are not persuasive to overcome the above rejection. While Examiner agrees that applicants have described 2-3 species of the enzyme, it should be noted that all three species are from a single source, i.e., *Sulfolobus solfataricus* strains. However, claims are drawn to enzymes isolated from all sources including all other microbes, plants and animals and variants, mutants and recombinants. Providing the assay for the enzyme (the trehaloseoligosaccharide-hydrolyzing activity) also is not persuasive to overcome the above rejection, because applicants have not taught as to how one skilled in the art should go ahead in identifying such strains and the specification does not provide a single universal method that could be used to isolate and characterize the enzyme without any undue experimentation. Applicants also argue that they have provided the base polynucleotide sequence and provide examples for preparation methods for chromosome DNAs and production of recombinant enzyme, DNA probes etc. and assay methods for trehaloseoligosaccharide-hydrolyzing activity. However, this is not persuasive because while methods to produce variants of a known sequence such as site-specific mutagenesis, random mutagenesis, etc. are well known

to the skilled artisan producing enzymes that read on enzymes from all sources including variants, mutants and recombinants as claimed by applicants requires that one of ordinary skill in the art know or be provided with guidance for the selection of which of the infinite number of variants have the claimed property. Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities. This would clearly constitute undue experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has not been provided in the instant specification. As previously stated the specification does not establish: (A) a rational and predictable scheme for isolation and characterization of the above enzyme from any or all sources including any microbe, plant or animal; (B) regions of the protein structure which may be modified without effecting its activity; (C) the general tolerance of such polypeptides to modification and extent of such tolerance; (D) a rational and predictable scheme for modifying any residue in those polypeptides with an expectation of obtaining the desired biological function; and (E) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Therefore, the above rejection is maintained.

Claims 25-36 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 25-36 are directed to polypeptides which acts on a substrate saccharide composed of at least three sugar units wherein at least three sugar units from the reducing end are glucose residues so as to liberate principally monosaccharides and/or disaccharides by hydrolyzing the substrate saccharide from the reducing end side isolated from all or any source including variants, mutants and recombinants. Claims 25-34 are rejected under this section of 35 USC 112 because the claims are directed to a genus of polypeptides that have not been described in the specification. No description has been provided of all the polypeptides including the modified polypeptide sequences encompassed by the claim. No information, beyond the characterization of SEQ ID NO:6 and 8 has been provided by applicants which would indicate that they had possession of the claimed genera of polypeptides. The specification does not contain any disclosure of the structure of all the polypeptide sequences encompassed by the claims. The genera of polypeptides claimed are large variable genera including peptides which can have a wide variety of structures. Therefore many structurally unrelated polypeptides are encompassed within the scope of these claims. The specification discloses only two species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

In response to the previous Office action, applicants traverse the above rejection and argue on similar grounds as they have argued for the enablement rejection. Specifically applicants argue that in pages 56 and 57, the term "equivalent sequence" is described as the amino acid sequence of SEQ ID NO:6 and 8 but containing insertions, replacements or deletions of some amino acids yet retaining amylase activity. While this may be so, applicants fail to recognize that they have not actually described the primary structure of all those polypeptides in which amino acids have been modified. Applicants submit that the present specification provides sufficient description to allow one skilled in the art to carry out the present invention and that the specification indeed describes all the encompassed polypeptides. Examiner respectfully disagrees with such an argument. As discussed in the written description guidelines, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that the species which are adequately described are representative of the entire genus. **Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.** Satisfactory disclosure of a representative number depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed.

For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus. In the instant case the claimed genera of claims 25-34, 128, 150-151 includes species which are widely variant in structure. The genus of claims 25-34, 128, 150-151 is structurally diverse as it encompasses polypeptides with the unique trehaloseoligosaccharide-hydrolyzing activity. As such, neither the description of the structure and function of SEQ ID NOS:6 and 8 nor the disclosure solely of functional features present in all members of the genus is sufficient to be representative of the attributes and features of the entire genus. Hence the above rejection is maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 123-128, 151-153 are rejected under 35 U.S.C. 102(b) as being anticipated by Lama et al. (Biotechnology Forum. Eur., 1991, Vol. 8(4):201-203). This rejection is based upon the public availability of a printed publication. Claims 123-128, 151-153 of the instant application are drawn to an amylase which acts on a substrate saccharide composed of at least three sugar units wherein the last three sugar units from the reducing end are glucose residues so as to liberate principally monosaccharides and/or disaccharides by hydrolyzing the substrate from the reducing end side and the linkage between the first and the second glucose residues from the

reducing end side is α-1, α-1 while the linkage between the second and the third glucose residues from the reducing end side is α-1,4 so as to liberate α, α-trehalose by hydrolyzing the α-1,4 linkage between the second and the third glucose residues, wherein the enzyme has its optimum temperature for its action between 60 to 85°C, wherein the polypeptide of the enzyme comprises SEQ ID NO:6 or 8 encoded by a polynucleotide represented by SEQ ID NO:5 or nucleotides 642-2315 of SEQ ID NO:5 or a polynucleotide which is capable of hybridizing to the above polynucleotides at 65° C overnight in a 6XSSPE/0.5% SDS buffer or encoded by a polynucleotide represented by SEQ ID NO:7 or nucleotides 1176-2843 of SEQ ID NO:7 or a polynucleotide which is capable of hybridizing to the above polynucleotides at 65° C overnight in a 6XSSPE/0.5% SDS. Lama et al. disclose an identical preparation of the enzyme isolated from the very same source i.e., *S.solfataricus.* Lama et al. describe an enzyme which acts on a substrate saccharide composed of at least three sugar units wherein the last three sugar units from the reducing end are glucose residues so as to liberate principally monosaccharides and/or disaccharides by hydrolyzing the substrate from the reducing end side and the linkage between the first and the second glucose residues from the reducing end side is α-1, α-1 while the linkage between the second and the third glucose residues from the reducing end side is α-1,4 so as to liberate α, α-trehalose by hydrolyzing the α-1,4 linkage between the second and the third glucose residues. Lama et al. also describe the enzyme as a thermophilic enzyme wherein the enzyme has an optimum temperature range of 60-85 ° C. The reference does not explicitly teach the amino acid sequence of the enzyme as depicted in SEQ ID NO:6 or 8 or that it is encoded by a polynucleotide as represented in SEQ ID NO:5 or nucleotides 642-2315 of SEQ ID NO:5 or encoded by SEQ ID NO:7 or nucleotides 1176-2843 of SEQ ID NO:7or polynucleotides capable

of hybridizing to the above polynucleotides at 65° C overnight in a 6XSSPE/0.5% SDS buffer. However, judging from all the other similarities between the enzyme of the reference and the enzyme claimed in the instant application, such characteristics including the amino acid sequence (SEQ ID NO:6 or 8) would be inherent characteristics of the said enzyme. Therefore Lama et al. anticipate claims 123-128, 151-153 of this application as written.

Since the Office does not have the facilities for examining and comparing applicants' protein with the protein of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same material structural and functional characteristics of the claimed protein). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 25-36, 150 are rejected under 35 U.S.C. 103(a) as obvious over Lama et al. (Biotechnology Forum. Eur., 1991, Vol. 8(4):201-203). This rejection is based upon the public availability of a printed publication. Claims 25-36, 150 of the instant application are drawn to an amylase which acts on a substrate saccharide composed of at least three sugar units wherein the last three sugar units from the reducing end are glucose residues so as to liberate principally

monosaccharides and/or disaccharides by hydrolyzing the substrate from the reducing end side and shows a trehaloseoligosaccharide-hydrolyzing activity of more than 10.6 units/mg, wherein the linkage between the first and the second glucose residues from the reducing end side is α-1, α-1 while the linkage between the second and the third glucose residues from the reducing end side is α-1,4 so as to liberate α, α-trehalose by hydrolyzing the α-1,4 linkage between the second and the third glucose residues, wherein said enzyme also has endotype-hydrolyzing activity, wherein the molecular weight of the enzyme is between 61,000 to 64,000, wherein the enzyme has an optimum pH range of pH 4.5-5.5, temperature range of 60-85 ° C and a pH stability in the range of pH 3.0 to 13.0 and a thermostability of 100% (activity) even after exposure at 80 ° C to 85 ° C for 6 hours, an isoelectric point of pH 4.3 to 5.4, wherein the enzyme is inhibited by 5 mM of Cu salt and wherein the enzyme is derived from a bacteria belonging to *Sulfolobales*, belonging to the genus *S.solfataricus* strain KM1, DSM 5833, and wherein the polypeptide of the enzyme comprises SEQ ID NO:6 or 8 or an equivalent sequence thereof, wherein the polypeptide comprises a methionine at the N-terminus and has an optimum temperature between 60 to 85 ° C. Lama et al. teach a similar preparation of the enzyme isolated from the very same source i.e., *S.solfataricus* . Lama et al. describe an enzyme which acts on a substrate saccharide composed of at least three sugar units wherein the last three sugar units from the reducing end are glucose residues so as to liberate principally monosaccharides and/or disaccharides by hydrolyzing the substrate from the reducing end side and the linkage between the first and the second glucose residues from the reducing end side is α-1, α-1 while the linkage between the second and the third glucose residues from the reducing end side is α-1,4 so as to liberate α, α-trehalose by hydrolyzing the α-1,4 linkage between the second and the third glucose residues.

Lama et al. also describe the enzyme as a thermophilic enzyme wherein the enzyme has an optimum pH between pH 4.5-5.5, temperature range of 60-85 ° C and a pH stability in the range of pH 4.0 to 10.0 and a thermostability of 100% (activity) even after exposure at 80 ° C for more than 5 hours. The reference does not teach explicitly the isoelectric point of the enzyme as pH 4.3 to 5.4 or that the enzyme is inhibited by 5 mM of CuSO4 but the reference does teach that the enzyme is inhibited by 4 mM of CuCl2. The reference does not teach that the pH stability was within the range of pH 3.0 to 13.0.

However, with the reference of Lama et al. in hand, it would have been obvious to one of ordinary skill in the art to use the partially purified enzyme from Lama et al. and further purify it using the well established protein purification techniques available to those skilled in the art at the time of filing of this application and arrive at an enzyme preparation that has a higher specific activity such as 10.6 units/mg or further test the enzyme for its stability at a higher pH range such as 3-13.0 or thermal stability ranging from 60-85° C. As such it is the Examiner's position that if the polypeptide of Lama et al. had indeed been further purified or tested for pH stability between pH 3.0 to 13.0 or the thermal stability between 80-85 ° C for 6 hours, the reference enzyme would have tested the same as the enzyme in the instant invention with similar or identical specific activity and stability. One of ordinary skill in the art would have been motivated to purify and characterize the enzyme further as Lama et al. teach the biotechnological importance of the enzyme in the preparation of trehalose which has commercial uses in food and pharmaceutical industry. One of ordinary skill in the art would have a reasonable expectation of success since Lama et al. teach a reasonably purified enzyme and the art is rich in many

established methods of protein purification including variations of ion-exchange method of purification, methods for amino acid sequencing and methods for molecular cloning of proteins.

Therefore the above invention would have been *prima facie* obvious to one of ordinary skill in the art

In response to the previous Office action, applicants have traversed the above rejection (i.e. rejection 35 U.S.C. 102.b) by amending the claim 25 to recite a specific number for the specific activity of the enzyme. While submitting that Lama et al. have indeed obtained a similar enzyme from S.*solfataricus*, applicants argue that the reference teaches a partially purified enzyme whose specific activity was much lower than that claimed for the instant enzyme. Applicants also argue that the reference does not teach the amino acid sequence SEQ ID NO:6 or 8 as encoded by polynucleotides SEQ ID NO:5 or 7. Examiner respectfully maintains that such arguments are not persuasive to overcome the above rejection. In response to applicants amendment and arguments Examiner has rewritten the rejection arguing that the reference anticipates or renders them *prima facie* obvious to one of ordinary skill in the art.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath Rao whose telephone number is (703) 306-5681. The Examiner can normally be reached on M-F from 7:30 a.m. to 4:00 p.m. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, P.Achutamurthy, can be reached on (703) 308-3804. The fax number for Official Papers to Technology Center 1600 is (703) 305-3014. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Rebecca Prouty

REBECCA E. PROUTY
PRIMARY EXAMINER
1600

Manjunath N. Rao. Ph.D.
April 15, 2003